REMARKS

Claims 1-12, 17 and 19-21 are pending in the application. Claims 1-7, 9-11, 17, 19 and 20 stand withdrawn from consideration. Claims 8 and 21 have been amended, and Claim 12 remains as it stood in the previous office action. Claims 8, 12 and 21 stand rejected. Applicants address the rejections in the order in which they were presented in the office action.

Drawing Objection

Applicants acknowledge with appreciation the Examiner's acceptance of changes to the drawings presented in the last office action. However, the Examiner has raised an objection to Figure 2B. Submitted herewith for approval is a proposed amended drawing sheet for Figure 2B wherein the structure of R" has been amended as indicated in the office action. A copy of Figure 2B as filed in the last office action showing the above-identified changes in red ink can be found in the Appendix filed concurrently herewith. Applicants respectfully request approval of the amendments to this drawing. Upon approval of these changes, a corrected drawing will be submitted to the Official Draftsperson of the United States Patent and Trademark Office.

35 U.S.C. §112, Second Paragraph Rejection of Claim 21

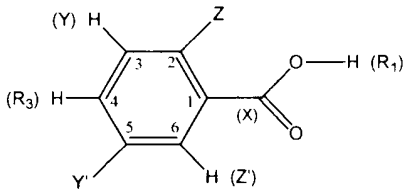
The Examiner rejected Claim 21 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which Applicants regard as the invention. As discussed in the office action, Applicants have amended Claim 21 to adopt the Examiner's suggested language "or a pharmaceutically acceptable salt thereof." Therefore, the Applicants respectfully request that the Examiner remove this rejection.

35 U.S.C. §102 (b) Rejection of Claims 8 and 12: Berger

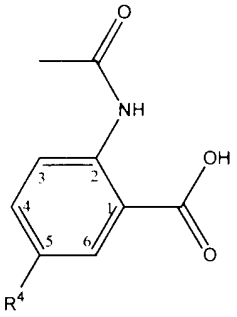
The Examiner rejected Claims 8 and 12 under 35 U.S.C. §102(b) as being anticipated by Berger, U.S. Patent 3,657,436 (the '436 patent).

Applicants have amended Claim 8 in view of another prior art rejection as discussed below. Upon further consideration of Berger, Applicants believe that the compounds recited

in Claim 8 are not disclosed by Berger. In one aspect, Berger teaches compounds having the following general structure provided immediately below on the right.



Claim 8 Compounds



N-Acetyl-5-substituted-anthranilic acid
Berger Compound (1)

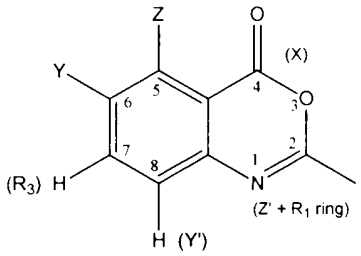
The Berger compound (1) discloses R^4 as hydrogen, halogen or lower alkoxy.

As shown in the table below, Claim 8 does not read on Berger's substituted aromatic compounds at the substituted or unsubstituted amino position.

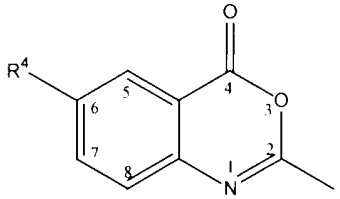
Claim 8	Berger
X is (C=O)O	(C=O)O at Position 1
R_1 is H	R^2 is H on the carboxyl at Position 1
Z′ is H (because Z cannot be H, Z′ must be at Position 6)	R^3 is H at Position 6
Y′ can be H or halogen at Position 5	R^4 can be H, halogen, or lower alkoxy
R_3 is H	H at Position 4
Y is H	H at Position 3
Z cannot be amino because if Z is NHR^{11}, R^{11} would have to be hydrogen, and in Claim 8, R^{11} cannot be hydrogen. **Z cannot be $NHCOR^6$ as recited by Berger because if Z is NHR^{11}, R^{11} would have to be a lower alkanoyl, and in Claim 8, R^{11} cannot be alkanoyl.**	at Position 2, NRR^1 wherein R is H and R^1 is H or lower alkanoyl NRR^1 is either amino or $NHCOR^6$ with R^6 being a lower alkyl of up to 6 carbons

Considering the comparative structures and the groups in the table above, Berger does not anticipate the compounds of Applicants' Claim 8. In Claim 8 Compounds, Z must be at Position 2 and Z′ at Position 6 because Z is not H in Claim 8 and H is provided at Position 6 of the Berger Compound (1). However, Z of Claim 8 does not recite the amino groups NRR^1 or $NHCOR^6$ at Position 2 as taught by Berger Compound (1) because when Z equals NHR^{11}, R^{11} cannot be H or the lower alkanoyl.

In another aspect, Berger teaches heterocyclic compounds where R, R^1 and R^2 when taken together are ethylidyne as provided immediately below on the right.



Claim 8 Compounds



2-methyl-6-substituted-4H-3,1-benzoxazin-4-one

Berger Compound (2)

Berger Compound (2) discloses R^4 as hydrogen, halogen or lower alkoxy.

As shown in the table below, Claim 8 does not read on Berger's substituted heterocyclic compounds; in particular, Applicant's Z cannot be hydrogen as recited by Berger.

Claim 8	Berger
Z' and R_1 collectively form a heterocyclic ring X is (C=O)O R_1 is C_1 alkyl Z' is amino	heterocyclic ring when R, R^1 and R^2 taken together are ethylidyne (C=O)O at Positions 4 and 3 C at Position 2 N at Position 1
Y' is H	H at Position 8
R_3 is H	H at Position 7
Y is H, halogen	R^4 is H, halogen or lower alkoxy
Z cannot be H as recited by Berger (because Z' is in the heterocyclic ring, Z must be the H at Position 5)	H at Position 5

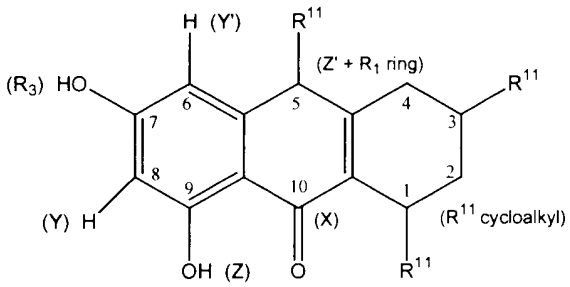
Considering the comparative structures and the groups in the table above, Berger does not anticipate the compounds of Applicants' Claim 8 because Z must be at Position 5 of Berger Compound (2). Applicants' Claim 8 does not recite hydrogen at Position 5 as taught by Berger.

For these reasons, Applicants respectfully request that the Examiner withdraw this 35 U.S.C. §102(b) rejection of Claim 8 in view of Berger. Additionally, because Claim 12 is dependent upon Claim 8, Applicants respectfully request that the Examiner withdraw this 35 U.S.C. §102(b) rejection of Claim 12 in view of Berger.

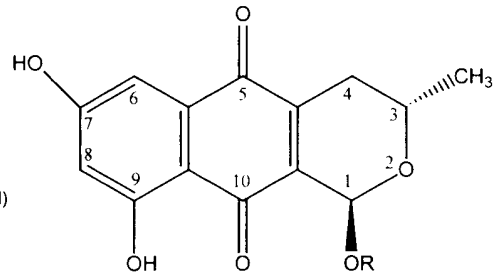
35 U.S.C. §102 (b) Rejection of Claims 8 and 12: Singh

The Examiner has rejected Claims 8 and 12 under 35 U.S.C. §102(b) as being anticipated by Singh, et al. *Tetrahedron Letters* 32:5279-5282 (1991) (Singh).

Applicants have amended Claim 8 in view of another prior art rejection as discussed below. Upon further consideration of Singh, Applicants believe that the compounds recited in Claim 8 are not disclosed by Singh. In one aspect, Singh teaches compounds having the following general structure provided immediately below on the right.



Claim 8 Compounds



thysanone

Singh Compound (1)

Singh Compound (1) discloses R as H or CH_3.

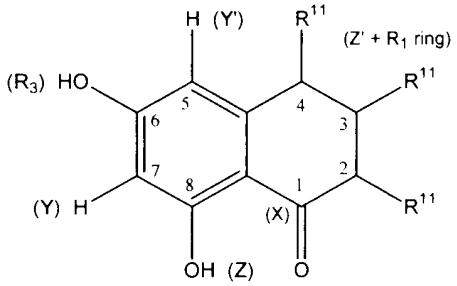
As shown in the table below, Claim 8 does not read on Singh's substituted heterocyclic compounds; in particular, Applicants' R^{11} cannot be oxo or a heterocyclic ring as recited by Singh.

Claim 8	Singh
X is (C=O) at Position 10 (Note: X cannot be C=O at Position 5 because Z would then be at Position 6 and Z cannot be H)	(C=O) at Position 10
Z' and R_1 can collectively form a carbocyclic ring which may be substituted with at least one R^{11} **R^{11} cannot be oxo** **R^{11} cannot be a heterocyclic ring**	carbocyclic ring including Positions 5 and 10 with substitutions of oxo group at Position 5, and the heterocyclic ring including Positions 1, 2, 3 and 4
Z is hydroxyl	OH at Position 9
Y is hydrogen	H at Position 8
R_3 is hydroxyl	OH at Position 7
Y' is hydrogen	H at Position 6

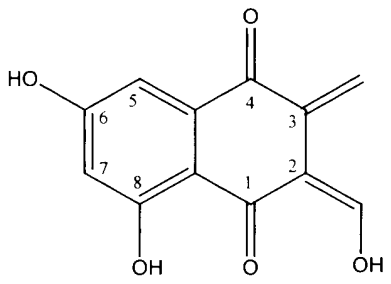
Considering the comparative structures and the groups in the table above, Singh does not anticipate the compounds of Applicants' Claim 8 because the carbocyclic ring formed by Z' and R^1 optionally substituted with one or more R^{11} in Applicants' Claim 8 does not recite an

oxo at Position 5 nor a heterocyclic ring including Positions 1, 2, 3, and 4 as taught by Singh Compound (1).

In another aspect, Singh discloses a compound having the following formula given immediately below on the right.



Claim 8 Compounds



substituted naphthoquinone

Singh Compound (2)

As shown in the table below, Claim 8 does not read on Singh Compound (2); in particular, Applicants' R^{11} cannot be a C_1 alkenyl at Positions 2 and 3 as disclosed by Singh.

Claim 8	Singh
X is (C=O) at Position 1 (Note: X cannot be C=O at Position 4 because Z would then be at the Position 5 and Z cannot be H)	(C=O) at Position 1
Z' and R_1 can collectively form a carbocyclic ring which may be substituted with at least one R^{11} **R^{11} cannot be oxo** **R^{11} cannot be substituted C_1 alkenyl as in Position 2 or unsubstituted C_1 alkenyl as in Position 3**	carbocyclic ring including Positions 1, 2, 3, and 4 with oxo at Position 4, substituted C_1 alkenyl at Position 2 and unsubstituted C_1 alkenyl at Position 3
Z is hydroxyl	OH at Position 8
Y is hydrogen	H at Position 7
R_3 is hydroxyl	OH at Position 6
Y' is hydrogen	H at Position 5

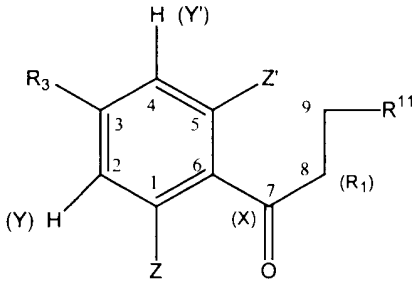
Considering the comparative structures and groups in the table above, Singh does not anticipate the compounds of Applicants' Claim 8 because the carbocyclic ring formed by Z' and R^1 optionally substituted with one or more R^{11} in Applicants' Claim 8 does not recite an oxo at Position 5 or a substituted or unsubstituted C_1 alkenyl at any position on the carbocyclic ring as taught by Singh.

For these reasons, Applicants respectfully request that the Examiner withdraw this 35 U.S.C. §102(b) rejection of Claim 8 in view of Singh. Additionally, because Claim 12 is dependent upon Claim 8, Applicants respectfully request that the Examiner withdraw this 35 U.S.C. §102(b) rejection of Claim 12 in view of Singh.

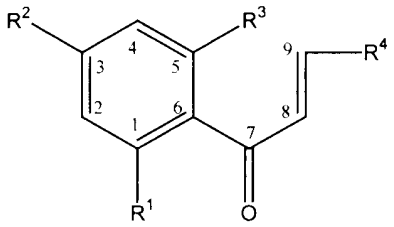
35 U.S.C. §102 (b) Rejection of Claims 8 and 12: Fujiu

The Examiner has rejected Claims 8 and 12 under 35 U.S.C. §102(b) as being anticipated by Fujiu, U.S. Patent No. 4,605,674 (hereinafter referred to as Fujiu).

Applicants have amended Claim 8 as discussed below. Applicants believe that the compounds recited in amended Claim 8 are not disclosed by Fujiu. In one aspect, Fujiu teaches compounds having the following general structure provided immediately below on the right.



Claim 8 Compounds



substituted propenone
Fujiu Compound

This Fujiu Compound discloses R^1 as hydroxy; R^2 as lower alkoxy; R^3 as hydrogen or lower alkoxy; and R^4 as phenyl which may be substituted by one or more substituents.

Upon consideration of Fujiu, Applicants have amended Claim 8 as discussed below.

Claim 8	Fujiu
X is (C=O)	(C=O) at Position 7
R_1 can be a saturated or unsaturated hydrocarbon from 1 to 10 carbons long which may be substituted with at least one R^{11} R^{11} can be an aryl which may be substituted, ***except when R_1 is an unsaturated hydrocarbon chain***	at Position 8 and 9, C_2 alkenyl substituted with R^4 being phenyl which may be substituted
Z is hydroxyl (Note: Z cannot be R^3 Position 5 because it cannot be hydrogen or lower alkoxy as defined by Fujiu)	R^1 at Position 1 is hydroxy
Y is H	H at Position 2
R_3 is O–C_1-C_{12} hydrocarbon	R^2 at Position 3 is lower alkoxy
Y' is H	H at Position 4
Z' can be C_1-C_3 alkoxy	R^3 is lower alkoxy

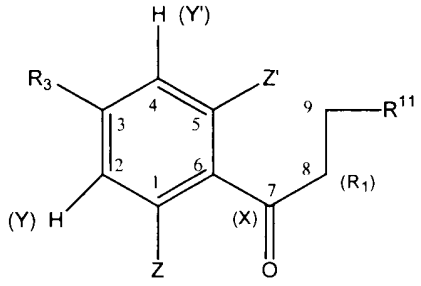
Applicants have amended Claim 8 to eliminate the possibility of having an unsaturated C_1-C_{10} hydrocarbon for R_1 being substituted with an aryl for R^{11}. In the specification, each instance of R_1 being a hydrocarbon substituted with R^{11} being an aryl shows R_1 as unsaturated (Formula VIII on Page 8, exemplary compounds in Example IV, and Fig. 2A). Fujiu does not anticipate compounds with a saturated hydrocarbon at Positions 8 and 9. Applicants believe that compounds recited in Claim 8 as amended are not disclosed by Fujiu.

For these reasons, Applicants respectfully request that the Examiner withdraw this 35 U.S.C. §102(b) rejection of Claim 8 in view of Fujiu. Additionally, because Claim 12 is dependent upon Claim 8, Applicants respectfully request that the Examiner withdraw this 35 U.S.C. §102(b) rejection of Claim 12 in view of Fujiu.

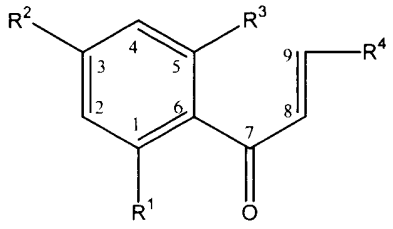
35 U.S.C. §102 (b) Rejection of Claims 8 and 12: Shinma

The Examiner has rejected Claims 8 and 12 under 35 U.S.C. §102(b) as being anticipated by Shinma, U.S. Patent No. 4,327,088 (hereinafter referred to as Shinma).

Applicants have amended Claim 8 as discussed herein. Applicants believe that the compounds recited in amended Claim 8 are not disclosed by Shinma. Shinma teaches compounds having the following general structure provided immediately below on the right.



Claim 8 Compounds



substituted propenones

Shinma Compound

This Shinma Compound discloses R^1 as hydroxy; R^2 and R^3 as lower alkoxy; and R^4 as phenyl which is substituted by acyloxy or alkoxyalkoxy.

Upon consideration of Shinma, Applicants have amended Claim 8 as discussed below.

Claim 8	Shinma
X is (C=O)	(C=O) at Position 7
R_1 can be a saturated or unsaturated hydrocarbon from 1 to 10 carbons long which may be substituted with at least one R^{11} R^{11} can be an aryl which may be substituted, ***except when R_1 is an unsaturated hydrocarbon chain***	at Position 8 and 9, C_2 alkenyl substituted with R^4 being phenyl which may be substituted
Z is hydroxyl (Z cannot be R^3 at Position 5 because Z cannot be lower alkoxy as recited by Shinma)	R^1 is hydroxy
Y is H	H at Position 2
R_3 is O–C_1-C_{12} hydrocarbon	R^2 is lower alkoxy
Y′ is H	H at Position 4
Z′ can be C_1-C_3 alkoxy	R^3 is lower alkoxy

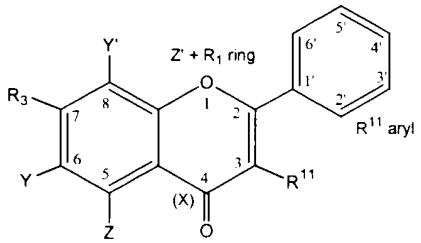
As mentioned above, Applicants have amended Claim 8 to eliminate the possibility of having an unsaturated C_1-C_{10} hydrocarbon for R_1 being substituted with an aryl for R^{11}. The chalcones and acrylophenones taught by Shinma do not anticipate compounds with a saturated hydrocarbon at Position 8 and 9. Applicants believe that compounds recited in Claim 8 as amended are not disclosed by Shinma.

Applicants respectfully request that the Examiner withdraw this 35 U.S.C. §102(b) rejection of Claim 8 in view of Shinma. Additionally, because Claim 12 is dependent upon Claim 8, Applicants respectfully request that the Examiner withdraw this 35 U.S.C. §102(b) rejection of Claim 12 in view of Shinma.

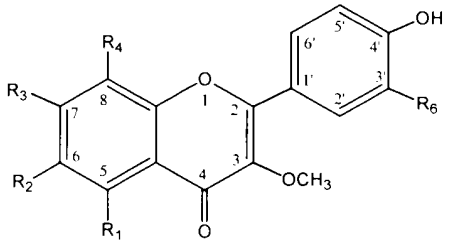
35 U.S.C. §102 (b) Rejection of Claims 8 and 12: De Meyer

The Examiner has rejected Claims 8 and 12 under 35 U.S.C. §102(b) as being anticipated by De Meyer.

Applicants have amended Claim 8 in view of prior art rejection as previously discussed. Applicants believe that the compounds recited in amended Claim 8 are not disclosed by De Meyer. In one aspect, De Meyer teaches compounds having the following general structure provided immediately below on the right.



Claim 8 Compounds



4'-hydroxy-3-methoxyflavones
De Meyer Group I

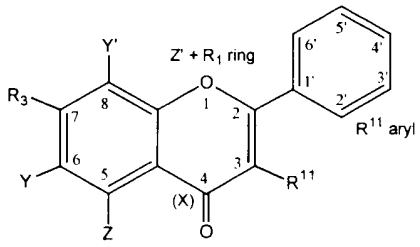
De Meyer Compound (1) discloses R_1 as H, OH, OCH_3 or CH_3; R_2 as H, OH, OCH_3, CH_3, $CH(CH_3)_2$, Cl, NO_2 or NH_2; R_3 as H, OH, OCH_3, CH_3, $CH(CH_3)_2$, Cl, Br, I or F; R_4 as H, CH_3 or OCH_3; and R_6 as H, OH or OCH_3.

As shown in the table below, Claim 8 does not read on this group of substituted 4-hydroxy-3-methoxyflavones (herein referenced as Group I) as taught by De Meyer.

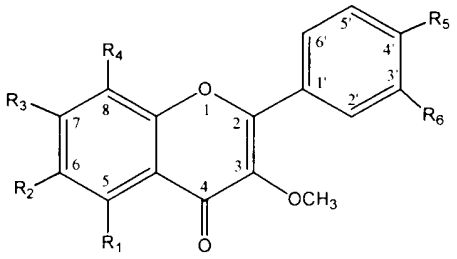
Claim 8	De Meyer; Group I (Compounds 1-35)
X is (C=O)	(C=O) at Position 4
Z' and R_1 can collectively form a heterocyclic ring which may be substituted with at least one R^{11} R^{11} can be substituted aryl **R^{11} cannot be methoxy**	heterocyclic ring including Positions 1, 2, 3, and 4 with the following substitutions: substituted phenyl at Position 2 methoxy at Position 3
Z is hydroxyl	R_1 is hydroxyl
Y is hydrogen, halogen, nitro or C_1-C_3 alkyl	R_2 is H, CH_3, $CH(CH_3)_2$, Cl or NO_2
R_3 is hydrogen, hydroxyl, C_1-C_{12} hydrocarbon, or O– C_1-C_{12} hydrocarbon	R_3 is H, OH, OCH_3, CH_3 or $CH(CH_3)_2$
Y' is hydrogen or C_1-C_3 alkyl	R_4 is H or CH_3

Considering the comparative structures and the groups in the table above, De Meyer Group I compounds do not anticipate the compounds of Applicants' Claim 8 because the carbocyclic ring formed by Z' and R^1 optionally substituted with one or more R^{11} in Applicants' Claim 8 does not recite a methoxy at Position 3 as taught by De Meyer.

In another aspect, De Meyer teaches compounds having the following general structure provided immediately below on the right.



Claim 8 Compounds



4'-substituted-3-methoxyflavones
De Meyer Group II

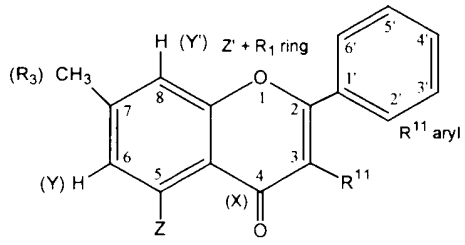
De Meyer Group II discloses R_1 as H, OH, OCH_3 or $OCOCH_3$; R_2 as H, OH, OCH_3 or Cl; R_3 as H, OH, OCH_3, CH_3, $OCOCH_3$ or Cl; R_4 as H or OCH_3; R_5 as OCH_3, Cl and $OCOCH_3$; and R_6 as H, OCH_3 or $OCOCH_3$.

As shown in the table below, Claim 8 does not read on this group of substituted 3-methoxyflavones (herein referenced as Group II) as taught by De Meyer.

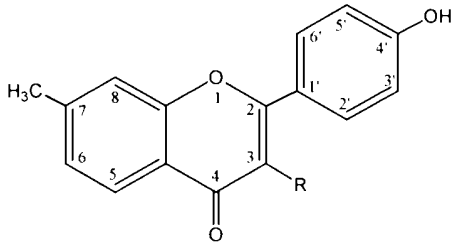
Claim 8	De Meyer; Group II (Compounds 36-57)
X is (C=O)	(C=O) at Position 4
Z' and R_1 can collectively form a heterocyclic ring which may be substituted with at least one R^{11} R^{11} can be substituted aryl **R^{11} cannot be methoxy**	heterocyclic ring including Positions 1, 2, 3 and 4with the following substitutions: substituted phenyl at Position 2 methoxy at Position 3
Z is hydroxyl	R_1 is hydroxyl
Y is hydrogen, halogen, nitro or C_1-C_3 alkyl	R_2 is H, CH_3, $CH(CH_3)_2$, Cl or NO_2
R_3 is hydrogen, hydroxyl, C_1-C_{12} hydrocarbon, or O-- C_1-C_{12} hydrocarbon	R_3 is H, OH, OCH_3, CH_3 or $CH(CH_3)_2$
Y' is hydrogen or C_1-C_3 alkyl	R_4 is H or CH_3

Considering the comparative structures and the groups in the table above, De Meyer Group II compounds do not anticipate the compounds of Applicants' Claim 8 because the carbocyclic ring formed by Z' and R^1 optionally substituted with one or more R^{11} in Applicants' Claim 8 does not recite a methoxy at Position 3 as taught by De Meyer.

In another aspect, De Meyer teaches compounds having the following general structure provided immediately below on the right.



Claim 8 Compounds



4'-hydroxy-7-methylflavones
De Meyer Group III

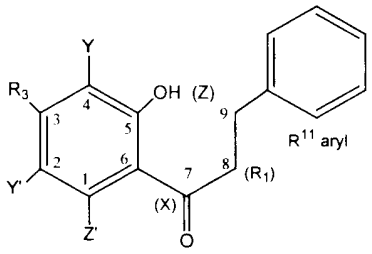
De Meyer Group III discloses R as Cl, CH_3, NH_2, $OCH(CH_3)_2$ or OC_2H_5.

As shown in the table below, Claim 8 does not read on De Meyer's 3-substituted-4-hydroxy-7-methylflavones.

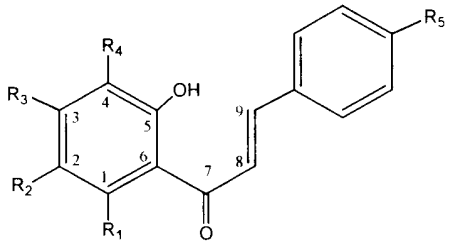
Claim 8	De Meyer; Group III (Compounds 58-62)
X is (C=O)	(C=O) at Position 4
Z' and R_1 can collectively form a heterocyclic ring which may be substituted with at least one R^{11} R^{11} can be substituted aryl R^{11} can be Cl, CH_3 or NH_2	heterocyclic ring including Positions 1, 2, 3 and 4 with the following substitutions: phenyl at Position 2 R at Position 3 can be Cl, CH_3 or NH_2
Z cannot be hydrogen	H at Position 5
Y can be hydrogen	H at Position 6
R_3 can be C_1-C_{12} hydrocarbon	CH_3 at Position 7
Y' can be hydrogen	H at Position 8

Considering the comparative structures and the groups in the table above, De Meyer Group III compounds do not anticipate the compounds of Applicants' Claim 8 because Z in Applicants' Claim 8 does not recite hydrogen at Position 3 as taught by De Meyer.

In yet another aspect, De Meyer teaches compounds having the following general structure provided immediately below on the right.



Claim 8 Compounds



substituted propenones
De Meyer Group IV

De Meyer Group IV discloses R_1 as H or OCH3; R_2 as H, OCH_3, CH_3, $CH(CH_3)_2$, $OCH_2C_6H_5$, Cl or NO_2; R_3 as H, CH_3, $CH(CH_3)_2$, OCH_3, $OCH_2C_6H_5$, Cl, Br, I or F; R_4 as H, OCH_3 or CH_3; and R_5 as OCH_3, $OCH_2C_6H_5$ or Cl.

As shown in the table below, Claim 8 does not read on De Meyer's 2-hydroxychalcones.

Claim 8	De Meyer; Group IV (Compounds 63-90)
X is (C=O)	(C=O) at Position 7
R_1 can be a saturated or unsaturated hydrocarbon from 1 to 10 carbons long which may be substituted with at least one R^{11} R^{11} can be an aryl which may be substituted, ***except when R_1 is an unsaturated hydrocarbon chain***	at Positions 8 and 9, C_2 alkenyl substituted with substituted the following: phenyl
Z' is hydroxyl or C_1-C_3 alkoxy	R_1 is hydroxy or OCH_3
Y' can be hydrogen, nitro, C_1-C_3 alkyl	R_2 is H, CH_3, $CH(CH_3)_2$ or NO_2
R_3 can be hydrogen, C_1-C_{12} hydrocarbon or O–C_1-C_{12} hydrocarbon	R_3 is H, CH_3, $CH(CH_3)_2$, OCH_3 or $OCH_2C_6H_5$
Y can be hydrogen or C_1-C_3 alkyl	R_4 is H or CH_3
Z can be hydroxyl	OH at Position 5

As mentioned above, Applicants have amended Claim 8 to eliminate the possibility of having an unsaturated C_1-C_{10} hydrocarbon for R_1 being substituted with an aryl for R^{11}. The flavones disclosed by De Meyer Group IV do not anticipate the compounds of the present invention, and the chalcones taught by De Meyer do not anticipate compounds with a saturated hydrocarbon at the Position 8 and 9. Applicants believe that compounds recited in Claim 8 as amended are not disclosed by De Meyer.

Applicants respectfully request that the Examiner withdraw this 35 U.S.C. §102(b) rejection of Claim 8 in view of De Meyer. Additionally, because Claim 12 is dependent upon Claim 8, Applicants respectfully request that the Examiner withdraw this 35 U.S.C. §102(b) rejection of Claim 12 in view of De Meyer.

CONCLUSION

For reasons delineated above, Applicants respectfully request the consideration of all pending claims and proposed drawings, and favorable action on the same.

With the exception of a Petition for Extension of Time, Applicants do not believe that any additional fees are necessary for filing this amendment. However, if this is in error, please deduct the necessary fees from the Sidley Austin Brown & Wood LLP Deposit Account No. 18-1260. A Petition for Extension of Time-Two Months has been filed concurrently herewith.

Respectfully submitted,

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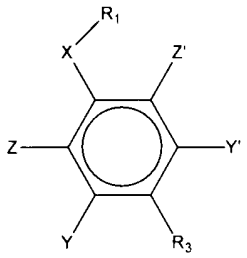
APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

The following is a marked-up version of the changes to the claims which are being made in the attached Amendment. Added material is underlined, and deleted material is bracketed.

IN THE CLAIMS

8. A method of inhibiting picornavirus activity, comprising contacting the picornavirus with a compound of the formula:



wherein

X is selected from the group consisting of C=O, S=O, C=S, (C=O)–NH, (C=O)–O and (C=O)–S:

R_1 is selected from the group consisting of:

(i) hydrogen or a hydrocarbon chain from 1 to about 10 carbons long selected from the group consisting of saturated, unsaturated and fluorinated, wherein said hydrocarbon chain is unsubstituted or substituted with at least one R^{11}, wherein R^{11} is selected from the group consisting of:

(ia) C_1-C_4 alkyl, C_2-C_4 alkenyl, C_3-C_8 cycloalkyl, <u>or</u> C_6-C_{10} bicycloalkyl [or aryl] which may be substituted or unsubstituted;

<u>(ib) aryl which may be substituted or unsubstituted, with the exception that R^{11} cannot be an aryl when R_1 is an unsaturated hydrocarbon chain;</u>

[(ib)] <u>(ic)</u> halogen, cyano, nitro, amino, hydroxy, adamantyl, carbamyl, carbamyloxy or keto;

[(ic)] <u>(id)</u> an oligopeptide of 1-3 amino acid residues; and

[(id)] <u>(ie)</u> $NR^{13}R^{14}$, CO_2R^{13}, $O(C{=}OR^{13})$, SO_2R^{14}, SOR^{14}, $(C{=}O)NR^{13}R^{14}$, or $NR^{14}(C{=}O)R^{13}$;

wherein:

R^{13} is selected from the group consisting of hydrogen, phenyl, benzyl, C_1-C_6 alkyl and C_3-C_6 alkoxyalkyl; and

R^{14} is selected from the group consisting of hydrogen, hydroxyl, and benzyl;

(ii) an oligopeptide or peptidomimetic molecule of 1 to 5 amino acids;

(iii) C_3-C_6 cycloalkyl, C_6-C_{10} bicycloalkyl, C_3-C_7 cycloalkylmethyl, or C_7-C_{10} arylalkyl, which may be additionally substituted with R^{11} as defined above;

R_3 is selected from the group consisting of:

(i) hydrogen, phenyl, hydroxyl, C_1-C_{12} hydrocarbon chain or O–C_1-C_{12} hydrocarbon chain which may be additionally substituted with at least one R^{11} as defined above; and

(ii) an oligopeptide of 1 to 3 amino acids joined to the backbone by an oxygen or a peptidomimetic;

Z is selected from the group consisting of hydroxyl, sulfhydryl, carboxyl and NHR^{11}, wherein R^{11} is defined as above;

Z' is selected from the group consisting of:

(i) hydroxyl, amino, carbamido, carbamyl, carbamyloxy or halogen;

(ii) hydrogen; and

(iii) C_1-C_4 alkyl, C_2-C_4 alkenyl, C_3-C_7 cycloalkenyl, or C_1-C_3 alkoxy which may be additionally substituted with at least one R^{11} as defined above;

alternatively Z' and R_1 collectively form a ring system selected from the group consisting of:

(a) C_5-C_8 carbocyclic ring which may be saturated or unsaturated, and which may be additionally substituted with at least one R^{11} as defined above; and

(b) C_5-C_{10} heterocyclic ring system which may be saturated or unsaturated and which includes at least one nitrogen, oxygen or sulfur atom, and which may be additionally substituted with at least one R^{11} as defined above;

Y and Y' are independently selected from the group consisting of:

(i) hydrogen, halogen, C_1-C_4 haloalkyl, or C_1-C_4 haloalkoxy;

(ii) carbamyl, carbamido, cyano, COR^{11}, vinyl, nitro, SO_2R^{11}, or SOR^{11} , wherein R^{11} is defined above;

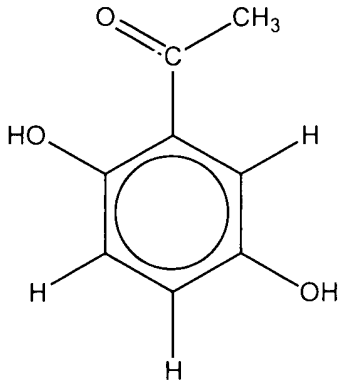
(iii) C_1-C_3 alkyl which may be additionally substituted with at least one R^{11} as defined above; and

(iv) an oligopeptide or a peptidomimetic of 1 to 3 amino acids;

and pharmaceutically acceptable salts thereof; with the proviso that when $X-R_1$ is a fluorinated keto acyl, Z is hydrogen;

for a time and under conditions effective to inhibit replication of said picornavirus.

21. A method of inhibiting picornavirus activity, comprising contacting the picornavirus with a compound of the formula:



[and] or a pharmaceutically acceptable [salts] salt thereof for a time and under conditions effective to inhibit replication of said picornavirus.

IN THE DRAWINGS

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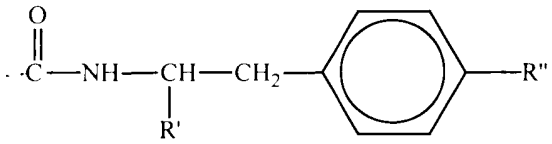
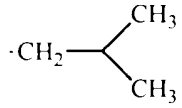
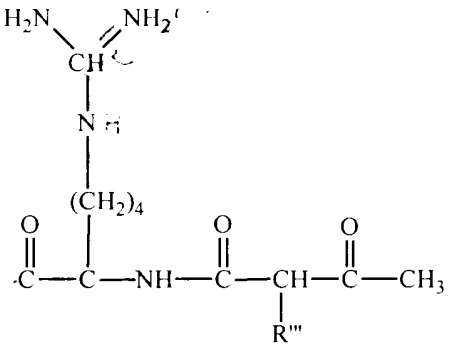
Figure 2B

3.

$R_2 =$ 

$R' =$  , $-CH_2-CH_3$, $-CH_3$, Or any branched aliphatic chain

$R'' =$ 

R''' = Small or branched aliphatic like side chain of Leu, Val, Ile or Ala